General

Guideline Title

Type 1 diabetes in adults: diagnosis and management.

Bibliographic Source(s)

National Clinical Guideline Centre. Type 1 diabetes in adults: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug 26. 86 p. (NICE guideline; no. 17).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Type 1 diabetes in adults. National clinical guideline for diagnosis and management in primary and secondary care. London (UK): Royal College of Physicians; 2004. 171 p. [382 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- April 8, 2016 – Metformin-containing Drugs : The U.S. Food and Drug Administration (FDA) is requiring labeling changes regarding the recommendations for metformin-containing medicines for diabetes to expand metformin's use in certain patients with reduced kidney function. The current labeling strongly recommends against use of metformin in some patients whose kidneys do not work normally. FDA concluded, from the review of studies published in the medical literature, that metformin can be used safely in patients with mild impairment in kidney function and in some patients with moderate impairment in kidney function.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC), which is based at the Royal College of Physicians, on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Note from NGC and NICE: In July 2016, NICE reworded the recommendation on screening for eye disease to clarify the role of general practitioners (GPs) in referring people for eye screening and also to add information on when this should happen. This change is reflected in the recommendations below.

Recommendations are marked as [new 2015], [2015], [2004], [2004, amended 2015] or [2004, amended 2016]:

- [new 2015] indicates that the evidence has been reviewed and the recommendation has been added or updated.
- [2015] indicates that the evidence has been reviewed but no change has been made to the recommended action.
- [2004] indicates that the evidence has not been reviewed since 2004.
- [2004, amended 2015] or [2004, amended 2016] indicates that the evidence has not been reviewed since 2004, but either changes have been made to the recommendation wording that change the meaning or NICE has made editorial changes to the original wording to clarify the action to be taken.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation), and is defined at the end of the "Major Recommendations" field.

Definitions for terms used in the guideline recommendations are detailed in the original guideline document.

Diagnosis and Early Care Plan

Diagnosis

Diagnose type 1 diabetes on clinical grounds in adults presenting with hyperglycaemia, bearing in mind that people with type 1 diabetes typically (but not always) have one or more of:

- Ketosis
- Rapid weight loss
- Age of onset below 50 years
- Body mass index (BMI) below 25 kg/m^2
- Personal and/or family history of autoimmune disease [new 2015]

Do not discount a diagnosis of type 1 diabetes if an adult presents with a BMI of 25 kg/m^2 or above or is aged 50 years or above. [new 2015]

Do not measure C-peptide and/or diabetes-specific autoantibody titres routinely to confirm type 1 diabetes in adults. [new 2015]

Consider further investigation in adults that involves measurement of C-peptide and/or diabetes-specific autoantibody titres if:

- Type 1 diabetes is suspected but the clinical presentation includes some atypical features (for example, age 50 years or above, BMI of 25 kg/m^2 or above, slow evolution of hyperglycaemia or long prodrome) or
- Type 1 diabetes has been diagnosed and treatment started but there is a clinical suspicion that the person may have a monogenic form of diabetes, and C-peptide and/or autoantibody testing may guide the use of genetic testing or
- Classification is uncertain, and confirming type 1 diabetes would have implications for availability of therapy (for example, continuous subcutaneous insulin infusion [CSII or 'insulin pump'] therapy). [new 2015]

When measuring C-peptide and/or diabetes-specific autoantibody titres, take into account that:

- Autoantibody tests have their lowest false negative rate at the time of diagnosis, and that the false negative rate rises thereafter
- C-peptide has better discriminative value the longer the test is done after diagnosis
- With autoantibody testing, carrying out tests for 2 different diabetes-specific autoantibodies, with at least 1 being positive, reduces the false negative rate [new 2015]

Early Care Plan

At the time of diagnosis (or if necessary after the management of critically decompensated metabolism), the diabetes professional team should

develop with and explain to the adult with type 1 diabetes a plan for their early care. To agree such a plan will generally require:

- Medical assessment to:
  - Ensure security of diagnosis of type of diabetes
  - Ensure appropriate acute care is given when needed
  - Review and detect potentially confounding disease and medicines
  - Detect adverse vascular risk factors
- Environmental assessment to understand:
  - The social, home, work and recreational circumstances of the person and carers
  - Their preferences in nutrition and physical activity
  - Other relevant factors, such as substance use
- Cultural and educational assessment to identify prior knowledge and to enable optimal advice and planning about:
  - Treatment modalities
  - Diabetes education programmes
- Assessment of emotional state to determine the appropriate pace of education

The results of the assessment should be used to agree a future care plan. Some items of the initial diabetes assessment:

- Acute medical history
- Social, cultural and educational history/lifestyle review
- Complications history/symptoms
- Long-term/recent diabetes history
- Other medical history/systems
- Family history of diabetes/cardiovascular disease
- Medication history/current medicines
- Vascular risk factors
- Smoking
- General examination
- Weight/BMI
- Foot/eye/vision examination
- Urine albumin excretion/urine protein/serum creatinine
- Psychological wellbeing
- Attitudes to medicine and self-care
- Immediate family and social relationships and availability of informal support [2004]

Elements of an individualised and culturally appropriate plan will include:

- Sites and timescales of diabetes education, including nutritional advice (see "Education and Information" below)
- Initial treatment modalities, including guidance on insulin injection and insulin regimens (see "Insulin Therapy" and "Insulin Delivery" below)
- Means of self-monitoring and targets (see "Blood Glucose Measurement" below)
- Symptoms, risk and treatment of hypoglycaemia
- Management of special situations, such as driving
- Means and frequency of communication with the diabetes professional team
- Management of cardiovascular risk factors (see "Control of Cardiovascular Risk" below)
- For women of childbearing potential, implications for pregnancy and family planning advice (see the NGC summary of the NICE guideline Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period)
- Frequency and content of follow-up consultations, including review of glycated haemoglobin (HbA1c) levels and experience of hypoglycaemia, and annual review [2004, amended 2015]

After the initial plan is agreed, put arrangements in place to implement it without inappropriate delay, and to provide for feedback and modification of the plan over the ensuing weeks. [2004]

Support and Individualised Care

Take account of any disabilities, including visual impairment, when planning and delivering care for adults with type 1 diabetes. [new 2015]

Advice to adults with type 1 diabetes should be provided by a range of professionals with skills in diabetes care working together in a coordinated

approach. A common environment (diabetes centre) is an important resource in allowing a diabetes multidisciplinary team to work and communicate efficiently while providing consistent advice. [2004]

Provide adults with type 1 diabetes with:

- Open-access services on a walk-in and telephone-request basis during working hours
- A helpline staffed by people with specific diabetes expertise on a 24-hour basis
- Contact information for these services [2004]

Regard each adult with type 1 diabetes as an individual, rather than as a member of any cultural, economic or health-affected group (see also "Dietary Advice" about the cultural preferences of individual adults with type 1 diabetes). [2004, amended 2015]

Set up an individual care plan jointly agreed with the adult with type 1 diabetes, review it annually and modify it taking into account changes in the person's wishes, circumstances and medical findings, and record the details. The plan should include aspects of:

- Diabetes education, including nutritional advice (see "Education and Information" and "Dietary Management" below)
- Insulin therapy, including dose adjustment (see "Insulin Delivery" and "Referral for Islet or Pancreas Transplantation" below)
- Self-monitoring (see "Blood Glucose Management" below)
- Avoiding hypoglycaemia and maintaining awareness of hypoglycaemia
- For women of childbearing potential, family planning, contraception and pregnancy planning (see the NGC summary of the NICE guideline Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period)
- Cardiovascular risk factor monitoring and management (see "Control of Cardiovascular Risk" below)
- Complications monitoring and management (see "Managing Complications" below)
- Means and frequency of communicating with the diabetes professional team
- Frequency and content of follow-up consultations, including review of HbA1c levels and experience of hypoglycaemia, and next annual review [2004, amended 2015]

Use population, practice-based and clinic diabetes registers (as specified by the National service framework for diabetes) to assist programmed recall for annual review and assessment of complications and cardiovascular risk. [2004]

The multidisciplinary team approach should be available to inpatients with type 1 diabetes, regardless of the reason for admission (see "Care of Adults with Type 1 Diabetes in Hospital" below). [2004]

At the time of diagnosis and periodically thereafter, provide adults with type 1 diabetes with up-to-date information about diabetes support groups (local and national), how to contact them and the benefits of membership. [2004]

Education and Information

Recommendations in this section update and replace the NICE technology appraisal guidance on the use of patient-education models for diabetes for adults with type 1 diabetes.

Offer all adults with type 1 diabetes a structured education programme of proven benefit, for example the DAFNE (dose-adjustment for normal eating) programme . Offer this programme 6 to 12 months after diagnosis. [new 2015]

If a structured education programme has not been undertaken by an adult with type 1 diabetes by 12 months after diagnosis, offer it at any time that is clinically appropriate and suitable for the person, regardless of duration of type 1 diabetes. [new 2015]

Provide an alternative of equal standard for any adult with type 1 diabetes unable or unwilling to participate in group education. [new 2015]

Ensure that any structured education programme for adults with type 1 diabetes includes the following components:

- It is evidence-based, and suits the needs of the person.
- It has specific aims and learning objectives, and supports the person and their family members and carers in developing attitudes, beliefs, knowledge and skills to self-manage diabetes.
- It has a structured curriculum that is theory-driven, evidence-based and resource-effective, has supporting materials, and is written down.
- It is delivered by trained educators who have an understanding of educational theory appropriate to the age and needs of the person, and who are trained and competent to deliver the principles and content of the programme.
- It is quality assured, and reviewed by trained, competent, independent assessors who measure it against criteria that ensure consistency.
- The outcomes are audited regularly. [new 2015]

Explain to adults with type 1 diabetes that structured education is an integral part of diabetes care. [new 2015]

Provide information about type 1 diabetes and its management to adults with type 1 diabetes at all opportunities from diagnosis onwards. Follow the principles in the NICE guideline on Patient experience in adult NHS services. [new 2015]

Consider the Blood Glucose Awareness Training (BGAT) programme for adults with type 1 diabetes who are having recurrent episodes of hypoglycaemia (see also "Awareness and Management of Hypoglycaemia" below). [new 2015]

Carry out more formal review of self-care and needs annually in all adults with type 1 diabetes. Vary the agenda addressed each year according to the priorities agreed between the healthcare professional and the adult with type 1 diabetes. [2004, amended 2015]

Dietary Management

Carbohydrate Counting

Offer carbohydrate-counting training to adults with type 1 diabetes as part of structured education programmes for self-management (see "Education and Information" above). [new 2015]

Consider carbohydrate-counting courses for adults with type 1 diabetes who are waiting for a more detailed structured education programme or are unable to take part in a stand-alone structured education programme. [new 2015]

Glycaemic Index Diets

Do not advise adults with type 1 diabetes to follow a low glycaemic index diet for blood glucose control. [new 2015]

Dietary Advice

Offer dietary advice to adults with type 1 diabetes about issues other than blood glucose control, such as weight control and cardiovascular risk management, as indicated clinically. [new 2015]

Provide nutritional information sensitive to personal needs and culture from the time of diagnosis of type 1 diabetes. [2004]

Provide nutritional information individually and as part of a diabetes education programme (see "Education and Information" above). Include advice from professionals with specific and approved training and continuing accredited education in delivering nutritional advice to people with health conditions. Offer opportunities to receive nutritional advice at intervals agreed between adults with type 1 diabetes and their advising professionals. [2004]

Discuss the hyperglycaemic effects of different foods an adult with type 1 diabetes wishes to eat in the context of the insulin preparations chosen to match those food choices. [2004]

Make programmes available to adults with type 1 diabetes to enable them to make:

- Optimal choices about the variety of foods they wish to consume
- Insulin dose changes appropriate to reduce glucose excursions when taking different quantities of those foods [2004, amended 2015]

Agree the choice of content, timing and amount of snacks between meals or at bedtime available to the adult with type 1 diabetes, based on informed discussion about the extent and duration of the effects of eating different food types and the insulin preparations available to match them. Modify those choices based on discussion of the results of self-monitoring tests. [2004]

Make information available on:

- Effects of different alcohol-containing drinks on blood glucose excursions and calorie intake
- Use of high-calorie and high-sugar 'treats' [2004, amended 2015]

Make information available about the benefits of healthy eating in reducing cardiovascular risk as part of dietary education in the period after diagnosis, and according to need and interest at intervals thereafter. Include information about fruit and vegetables, types and amounts of fat, and ways of making the appropriate nutritional changes. [2004, amended 2015]

Modify nutritional recommendations to adults with type 1 diabetes to take account of associated features of diabetes, including:

- Excess weight and obesity
- Underweight

- Eating disorders
- Hypertension
- Renal failure [2004]

Be aware of appropriate nutritional advice on common topics of concern and interest to adults living with type 1 diabetes, and be prepared to seek advice from colleagues with more specialised knowledge. Suggested common topics include:

- Body weight, energy balance and obesity management
- Cultural and religious diets, feasts and fasts
- Foods sold as 'diabetic'
- Sweeteners
- Dietary fibre intake
- Protein intake
- Vitamin and mineral supplements
- Alcohol
- Matching carbohydrate, insulin and physical activity
- Salt intake in hypertension
- Comorbidities, including nephropathy and renal failure, coeliac disease, cystic fibrosis or eating disorders
- Use of peer support groups [2004, amended 2015]

Physical Activity

Advise adults with type 1 diabetes that physical activity can reduce their enhanced cardiovascular risk in the medium and longer term. [2004]

Give adults with type 1 diabetes who choose to integrate increased physical activity into a more healthy lifestyle information about:

- Appropriate intensity and frequency of physical activity
- Role of self-monitoring of changed insulin and/or nutritional needs
- Effect of activity on blood glucose levels (likely fall) when insulin levels are adequate
- Effect of exercise on blood glucose levels when hyperglycaemic and hypoinsulinaemic (risk of worsening of hyperglycaemia and ketonaemia)
- Appropriate adjustments of insulin dosage and/or nutritional intake for exercise and post-exercise periods, and the next 24 hours
- Interactions of exercise and alcohol
- Further contacts and sources of information [2004]

Blood Glucose Management

HbA1c Measurement and Targets

Measurement

Measure HbA1c levels every 3 to 6 months in adults with type 1 diabetes. [new 2015]

Consider measuring HbA1c levels more often in adults with type 1 diabetes if the person's blood glucose control is suspected to be changing rapidly; for example, if the HbA1c level has risen unexpectedly above a previously sustained target. [new 2015]

Use methods to measure HbA1c that have been calibrated according to International Federation of Clinical Chemistry (IFCC) standardisation. [new 2015]

Inform adults with type 1 diabetes of their HbA1c results after each measurement and ensure that their most recent result is available at the time of consultation. Follow the principles in the NICE guideline on Patient experience in adult NHS services about communication. [new 2015]

If HbA1c monitoring is invalid because of disturbed erythrocyte turnover or abnormal haemoglobin type, estimate trends in blood glucose control using one of the following:

- Fructosamine estimation
- Quality-controlled blood glucose profiles
- Total HbA1c estimation (if abnormal haemoglobins) [2015]

Targets

Support adults with type 1 diabetes to aim for a target HbA1c level of 48 mmol/mol (6.5%) or lower, to minimise the risk of long-term vascular complications. [new 2015]

Agree an individualised HbA1c target with each adult with type 1 diabetes, taking into account factors such as the person's daily activities, aspirations, likelihood of complications, comorbidities, occupation and history of hypoglycaemia. [new 2015]

Ensure that aiming for an HbA1c target is not accompanied by problematic hypoglycaemia in adults with type 1 diabetes. [new 2015]

Diabetes services should document the proportion of adults with type 1 diabetes in a service who achieve an HbA1c level of 53 mmol/mol (7%) or lower. [new 2015]

Self-Monitoring of Blood Glucose

Frequency of Self-Monitoring of Blood Glucose

Advise routine self-monitoring of blood glucose levels for all adults with type 1 diabetes, and recommend testing at least 4 times a day, including before each meal and before bed. [new 2015]

Support adults with type 1 diabetes to test at least 4 times a day, and up to 10 times a day if any of the following apply:

- The desired target for blood glucose control, measured by HbA1c level (see "Targets" above), is not achieved
- The frequency of hypoglycaemic episodes increases
- There is a legal requirement to do so (such as before driving, in line with the Driver and Vehicle Licensing Agency (DVLA) At a glance guide to the current medical standards of fitness to drive)
- During periods of illness
- Before, during and after sport
- When planning pregnancy, during pregnancy and while breastfeeding (see the NGC summary of the NICE guideline Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period)
- If there is a need to know blood glucose levels more than 4 times a day for other reasons (for example, impaired awareness of hypoglycaemia, high-risk activities) [new 2015]

Enable additional blood glucose testing (more than 10 times a day) for adults with type 1 diabetes if this is necessary because of the person's lifestyle (for example, driving for a long period of time, undertaking high-risk activity or occupation, travel) or if the person has impaired awareness of hypoglycaemia. [new 2015]

Blood Glucose Targets

Advise adults with type 1 diabetes to aim for:

- A fasting plasma glucose level of 5 mmol/litre to 7 mmol/litre on waking and
- A plasma glucose level of 4 mmol/litre to 7 mmol/litre before meals at other times of the day [new 2015]

Advise adults with type 1 diabetes who choose to test after meals to aim for a plasma glucose level of 5 mmol/litre to 9 mmol/litre at least 90 minutes after eating. (This timing may be different in pregnancy – for guidance on plasma glucose targets in pregnancy, see the NGC summary of the NICE guideline Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period.) [new 2015]

Agree bedtime target plasma glucose levels with each adult with type 1 diabetes that take into account timing of the last meal and its related insulin dose, and are consistent with the recommended fasting level on waking (see recommendation above). [new 2015]

Empowering People to Self-Monitor Blood Glucose

Teach self-monitoring skills at the time of diagnosis and initiation of insulin therapy. [2004, amended 2015]

When choosing blood glucose meters:

- Take the needs of the adult with type 1 diabetes into account
- Ensure that meters meet current ISO standards [new 2015]

Educate adults with type 1 diabetes about how to measure their blood glucose level, interpret the results and know what action to take. Review

these skills at least annually. [new 2015]

Support adults with type 1 diabetes to make the best use of data from self-monitoring of blood glucose through structured education (see "Education and Information" above). [new 2015]

Sites for Self-Monitoring of Blood Glucose

Monitoring blood glucose using sites other than the fingertips cannot be recommended as a routine alternative to conventional self-monitoring of blood glucose. [2004, amended 2015]

Continuous Glucose Monitoring

Do not offer real-time continuous glucose monitoring routinely to adults with type 1 diabetes. [new 2015]

Consider real-time continuous glucose monitoring for adults with type 1 diabetes who are willing to commit to using it at least 70% of the time and to calibrate it as needed, and who have any of the following despite optimised use of insulin therapy and conventional blood glucose monitoring:

- More than 1 episode a year of severe hypoglycaemia with no obviously preventable precipitating cause
- Complete loss of awareness of hypoglycaemia
- Frequent (more than 2 episodes a week) asymptomatic hypoglycaemia that is causing problems with daily activities
- Extreme fear of hypoglycaemia
- Hyperglycaemia (HbA1c level of 75 mmol/mol [9%] or higher) that persists despite testing at least 10 times a day (see "Frequency of Self-Monitoring of Blood Glucose" above). Continue real-time continuous glucose monitoring only if HbA1c can be sustained at or below 53 mmol/mol (7%) and/or there has been a fall in HbA1c of 27 mmol/mol (2.5%) or more [new 2015]

For adults with type 1 diabetes who are having real-time continuous glucose monitoring, use the principles of flexible insulin therapy with either a multiple daily injection insulin regimen or continuous subcutaneous insulin infusion (CSII or insulin pump) therapy. [new 2015]

Real-time continuous glucose monitoring should be provided by a centre with expertise in its use, as part of strategies to optimise a person's HbA1c levels and reduce the frequency of hypoglycaemic episodes. [new 2015]

Insulin Therapy

Insulin Regimens

Offer multiple daily injection basal–bolus insulin regimens, rather than twice-daily mixed insulin regimens, as the insulin injection regimen of choice for all adults with type 1 diabetes. Provide the person with guidance on using multiple daily injection basal–bolus insulin regimens. [new 2015]

Do not offer adults newly diagnosed with type 1 diabetes non-basal–bolus insulin regimens (that is, twice-daily mixed, basal only or bolus only). [new 2015]

Long-Acting Insulin

Recommendations in this section update and replace the NICE technology appraisal guidance on the use of long-acting insulin analogues for the treatment of diabetes – insulin glargine, in relation to adults with type 1 diabetes.

Offer twice-daily insulin detemir as basal insulin therapy for adults with type 1 diabetes. [new 2015]

Consider, as an alternative basal insulin therapy for adults with type 1 diabetes:

- An existing insulin regimen being used by the person that is achieving their agreed targets
- Once-daily insulin glargine or insulin detemir if twice-daily basal insulin injection is not acceptable to the person, or once-daily insulin glargine if insulin detemir is not tolerated [new 2015]

Consider other basal insulin regimens for adults with type 1 diabetes only if the regimens in the recommendations above do not deliver agreed targets. When choosing an alternative insulin regimen, take account of the person's preferences and acquisition cost. [new 2015]

Continuous Subcutaneous Insulin Infusion (CSII or Insulin Pump) Therapy

For guidance on the use of continuous subcutaneous insulin infusion (CSII or insulin pump) therapy for adults with type 1 diabetes, see Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151). [new 2015]

Rapid-Acting Insulin

Offer rapid-acting insulin analogues injected before meals, rather than rapid-acting soluble human or animal insulins, for mealtime insulin replacement for adults with type 1 diabetes. [new 2015]

Do not advise routine use of rapid-acting insulin analogues after meals for adults with type 1 diabetes. [new 2015]

If an adult with type 1 diabetes has a strong preference for an alternative mealtime insulin, respect their wishes and offer the preferred insulin. [new 2015]

Mixed Insulin

Consider a twice-daily human mixed insulin regimen for adults with type 1 diabetes if a multiple daily injection basal–bolus insulin regimen is not possible and a twice-daily mixed insulin regimen is chosen. [new 2015]

Consider a trial of a twice-daily analogue mixed insulin regimen if an adult using a twice-daily human mixed insulin regimen has hypoglycaemia that affects their quality of life. [new 2015]

Optimising Insulin Therapy

For adults with erratic and unpredictable blood glucose control (hyperglycaemia and hypoglycaemia at no consistent times), rather than a change in a previously optimised insulin regimen, the following should be considered:

- Injection technique
- Injection sites
- Self-monitoring skills
- Knowledge and self-management skills
- Nature of lifestyle
- Psychological and psychosocial difficulties
- Possible organic causes such as gastroparesis [2004, amended 2015]

Give clear guidelines and protocols ('sick-day rules') to all adults with type 1 diabetes to help them to adjust insulin doses appropriately during periods of illness. [2004]

Adjuncts

Consider adding metformin to insulin therapy if an adult with type 1 diabetes and a BMI of 25 kg/m^2 (23 kg/m^2 for people from South Asian and related minority ethnic groups) or above wants to improve their blood glucose control while minimising their effective insulin dose. [new 2015]

Insulin Delivery

Adults with type 1 diabetes who inject insulin should have access to the insulin injection delivery device they find allows them optimal wellbeing, often using one or more types of insulin injection pen. [2004]

Provide adults with type 1 diabetes who have special visual or psychological needs with injection devices or needle-free systems that they can use independently for accurate dosing. [2004]

Offer needles of different lengths to adults with type 1 diabetes who are having problems such as pain, local skin reactions and injection site leakages. [new 2015]

After taking clinical factors into account, choose needles with the lowest acquisition cost to use with pre-filled and reusable insulin pen injectors. [new 2015]

Advise adults with type 1 diabetes to rotate insulin injection sites and avoid repeated injections at the same point within sites. [new 2015]

Provide adults with type 1 diabetes with suitable containers for collecting used needles and other sharps. Arrangements should be available for the suitable disposal of these containers. See also the section on "Safe Use and Disposal of Sharps" in the NGC summary of the NICE guideline Infection. Prevention and control of healthcare-associated infections in primary and community care. [2004, amended 2015]

Check injection site condition at least annually and if new problems with blood glucose control occur. [2004, amended 2015]

Referral for Islet or Pancreas Transplantation

Consider referring adults with type 1 diabetes who have recurrent severe hypoglycaemia that has not responded to other treatments (see "Awareness and Management of Hypoglycaemia" below) to a centre that assesses people for islet and/or pancreas transplantation. [new 2015]

Consider islet or pancreas transplantation for adults with type 1 diabetes with suboptimal diabetes control who have had a renal transplant and are currently on immunosuppressive therapy. [new 2015]

Awareness and Management of Hypoglycaemia

Identifying and Quantifying Impaired Awareness of Hypoglycaemia

Assess awareness of hypoglycaemia in adults with type 1 diabetes at each annual review. [new 2015]

Use the Gold score or Clarke score to quantify awareness of hypoglycaemia in adults with type 1 diabetes, checking that the questionnaire items have been answered correctly. [new 2015]

Explain to adults with type 1 diabetes that impaired awareness of the symptoms of plasma glucose levels below 3 mmol/litre is associated with a significantly increased risk of severe hypoglycaemia. [new 2015]

Strategies for Managing Impaired Awareness of Hypoglycaemia

Ensure that adults with type 1 diabetes with impaired awareness of hypoglycaemia have had structured education in flexible insulin therapy using basal–bolus regimens and are following its principles correctly. [new 2015]

Offer additional education focusing on avoiding and treating hypoglycaemia to adults with type 1 diabetes who continue to have impaired awareness of hypoglycaemia after structured education in flexible insulin therapy. [new 2015]

Avoid relaxing individualised blood glucose targets as a treatment for adults with type 1 diabetes with impaired awareness of hypoglycaemia. [new 2015]

If target blood glucose levels preferred by adults with type 1 diabetes who have impaired awareness of hypoglycaemia are lower than recommended, reinforce the recommended targets (see "Blood Glucose Targets" above). [new 2015]

Review insulin regimens and doses and prioritise strategies to avoid hypoglycaemia in adults with type 1 diabetes with impaired awareness of hypoglycaemia, including:

- Reinforcing the principles of structured education
- Offering continuous subcutaneous insulin infusion (CSII or insulin pump) therapy
- Offering real-time continuous glucose monitoring [new 2015]

If impaired awareness of hypoglycaemia is associated with recurrent severe hypoglycaemia in an adult with type 1 diabetes despite these interventions, consider referring the person to a specialist centre. [new 2015]

Preventing and Managing Hypoglycaemia

Explain to adults with type 1 diabetes that a fast-acting form of glucose is needed for the management of hypoglycaemic symptoms or signs in people who are able to swallow. [2004, amended 2015]

Adults with type 1 diabetes with a decreased level of consciousness as a result of hypoglycaemia and so are unable to take oral treatment safely should be:

- Given intramuscular glucagon by a family member or friend who has been shown how to use it (intravenous glucose may be used by healthcare professionals skilled in obtaining intravenous access)
- Monitored for response at 10 minutes, and then given intravenous glucose if their level of consciousness is not improving significantly
- Then given oral carbohydrate when it is safe to administer it, and placed under continued observation by a third party who has been warned of the risk of relapse [2004, amended 2015]

Explain to adults with type 1 diabetes that some hypoglycaemic episodes are an inevitable consequence of insulin therapy in most people using any insulin regimen, and that it is advisable that they should use a regimen that avoids or reduces the frequency of hypoglycaemic episodes while maintaining as optimal a level of blood glucose control as is feasible. Make advice available to all adults with type 1 diabetes to assist in obtaining the best such balance from any insulin regimen (see "Insulin Therapy" and "Insulin Delivery" above). [2004]

If hypoglycaemia becomes unusually problematic or of increased frequency, review the following possible contributory causes:

- Inappropriate insulin regimens (incorrect dose distributions and insulin types)
- Meal and activity patterns, including alcohol
- Injection technique and skills, including insulin resuspension if necessary
- Injection site problems
- Possible organic causes including gastroparesis
- Changes in insulin sensitivity (including drugs affecting the renin–angiotensin system and renal failure)
- Psychological problems
- Previous physical activity
- Lack of appropriate knowledge and skills for self-management [2004]

Manage nocturnal hypoglycaemia (symptomatic or detected on monitoring) by:

- Reviewing knowledge and self-management skills
- Reviewing current insulin regimen, evening eating habits and previous physical activity
- Choosing an insulin type and regimen that is less likely to induce low glucose levels at night [2004, amended 2015]

If early cognitive decline occurs in adults on long-term insulin therapy, supplement normal investigations by the consideration or investigation of possible brain damage resulting from overt or covert hypoglycaemia, and the need to ameliorate this. [2004]

Ketone Monitoring and Management of Diabetic Ketoacidosis (DKA)

Ketone Self-Monitoring for Prevention of DKA

Consider ketone monitoring (blood or urine) as part of 'sick-day rules' for adults with type 1 diabetes, to facilitate self-management of an episode of hyperglycaemia. [new 2015]

Ketone Monitoring in Hospital

In adults with type 1 diabetes presenting to emergency services, consider capillary blood ketone testing if:

- DKA is suspected or
- The person has uncontrolled diabetes with a period of illness, and urine ketone testing is positive. [new 2015]

Consider capillary blood ketone testing for inpatient management of DKA in adults with type 1 diabetes that is incorporated into a formal protocol. [new 2015]

Management of DKA

Professionals managing DKA in adults should be adequately trained, including regular updating, and be familiar with all aspects of its management which are associated with mortality and morbidity. These topics should include:

- Fluid balance
- Acidosis
- Cerebral oedema
- Electrolyte imbalance
- Disturbed interpretation of familiar diagnostic tests (white cell count, body temperature, electrocardiogram [ECG])
- Respiratory distress syndrome
- Cardiac abnormalities
- Precipitating causes
- Infection management, including opportunistic infections
- Gastroparesis
- Use of high dependency and intensive care units
- Recommendations immediately following in this section of the guideline

Management of DKA in adults should be in line with local clinical governance. [2004]

For primary fluid replacement in adults with DKA, use isotonic saline, not given too rapidly except in cases of circulatory collapse. [2004]

Do not generally use bicarbonate in the management of DKA in adults. [2004, amended 2015]

Give intravenous insulin by infusion to adults with DKA. [2004]

In the management of DKA in adults, once the plasma glucose concentration has fallen to 10 mmol/litre to 15 mmol/litre, give glucose-containing fluids (not more than 2 litres in 24 hours) in order to allow continued infusion of insulin at a sufficient rate to clear ketones (for example, 6 units/hour monitored for effect). [2004, amended 2015]

Begin potassium replacement early in DKA in adults, with frequent monitoring for the development of hypokalaemia. [2004]

Do not generally use phosphate replacement in the management of DKA in adults. [2004, amended 2015]

In adults with DKA whose conscious level is impaired, consideration should be given to inserting a nasogastric tube, monitoring urine production using a urinary catheter and giving heparin. [2004]

To reduce the risk of catastrophic outcomes in adults with DKA, ensure that monitoring is continuous and that review covers all aspects of clinical management at frequent intervals. [2004, amended 2015]

Associated Illness

In adults with type 1 diabetes who have a low BMI or unexplained weight loss, assess markers of coeliac disease. For guidance on testing for coeliac disease, see the NGC summary of the NICE guideline Coeliac disease: recognition, assessment and management. [2004, amended 2015]

Be alert to the possibility of the development of other autoimmune disease in adults with type 1 diabetes (including Addison's disease and pernicious anaemia). For advice on monitoring for thyroid disease, see "Thyroid Disease Monitoring" below. [2004, amended 2015]

Control of Cardiovascular Risk

Aspirin

Do not offer aspirin for the primary prevention of cardiovascular disease to adults with type 1 diabetes. [new 2015]

Identifying Cardiovascular Risk

Assess cardiovascular risk factors annually, including:

- Albuminuria
- Smoking
- Blood glucose control
- Blood pressure
- Full lipid profile (including high-density lipoprotein [HDL] and low-density lipoprotein [LDL] cholesterol and triglycerides)
- Age
- Family history of cardiovascular disease
- Abdominal adiposity [2004, amended 2015]

For guidance on tools for assessing risk of cardiovascular disease in adults with type 1 diabetes, see the recommendation in the NGC summary of the NICE guideline Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. [new 2015]

Interventions to Reduce Risk and Manage Cardiovascular Disease

For guidance on the primary prevention of cardiovascular disease in adults with type 1 diabetes, see the NGC summary of the NICE guideline Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. [new 2015]

Give adults with type 1 diabetes who smoke advice on smoking cessation and use of smoking cessation services, including NICE guidance-recommended therapies. Reinforce these messages annually for people who currently do not plan to stop smoking, and at all clinical contacts if there is a prospect of the person stopping. [2004]

Advise young adult non-smokers never to start smoking. [2004]

Provide intensive management for adults who have had myocardial infarction or stroke, according to relevant non-diabetes guidelines. In the

presence of angina or other ischaemic heart disease, beta-adrenergic blockers should be considered (for use of insulin in these circumstances, see "Care of Adults with Type 1 Diabetes in Hospital" below). For guidance on secondary prevention of myocardial infarction, see the NGC summary of the NICE guideline MI - secondary prevention. Secondary prevention in primary and secondary care for patients following a myocardial infarction. [2004, amended 2015]

Blood Pressure Management

Intervention levels for recommending blood pressure management should be 135/85 mmHg unless the adult with type 1 diabetes has albuminuria or 2 or more features of metabolic syndrome, in which case it should be 130/80 mmHg. See also "Diabetic Kidney Disease" below. [2004]

To allow informed choice by the person with hypertension, discuss the following with them:

- Reasons for choice of intervention level
- Substantial potential gains from small improvements in blood pressure control
- Possible negative consequences of therapy

See also "Diabetic Kidney Disease" below. [2004, amended 2015]

Start a trial of a renin–angiotensin system blocking drug as first-line therapy for hypertension in adults with type 1 diabetes. [2004, amended 2015]

Provide information to adults with type 1 diabetes on the potential for lifestyle changes to improve blood pressure control and associated outcomes, and offer assistance in achieving their aims in this area. [2004]

Do not allow concerns over potential side effects to inhibit advising and offering the necessary use of any class of drugs, unless the side effects become symptomatic or otherwise clinically significant. In particular:

- Do not avoid selective beta-adrenergic blockers where indicated in adults on insulin
- Low-dose thiazides may be combined with beta-blockers
- When calcium channel antagonists are prescribed, use only long-acting preparations
- Use direct questioning to detect the potential side effects of erectile dysfunction, lethargy and orthostatic hypotension with different drug classes [2004, amended 2015]

For guidance on blood pressure management in adults with type 1 diabetes and evidence of renal involvement, see the recommendations in the NGC summary of the NICE guideline Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care. [new 2015]

Care of Adults with Type 1 Diabetes in Hospital

Blood Glucose Control

Aim for a target plasma glucose level of 5 mmol/litre to 8 mmol/litre for adults with type 1 diabetes during surgery or acute illness. [new 2015]

Establish a local protocol for controlling blood glucose levels in adults with type 1 diabetes during surgery or acute illness to achieve the target level. [new 2015]

Use intravenous in preference to subcutaneous insulin regimens for adults with type 1 diabetes if:

- The person is unable to eat or is predicted to miss more than 1 meal or
- An acute situation is expected to result in unpredictable blood glucose levels – for example, major surgery, high-dose steroid treatment, inotrope treatment or sepsis or
- Insulin absorption is expected to be unpredictable, for example because of circulatory compromise[new 2015]

Consider continuing the person's existing basal insulin regimen (including basal rate if they are using continuous subcutaneous insulin infusion [CSII or insulin pump] therapy) together with protocol-driven insulin delivery for controlling blood glucose levels in adults with type 1 diabetes during surgery or acute illness. [new 2015]

Use subcutaneous insulin regimens (including rapid-acting insulin before meals) if an adult with type 1 diabetes and acute illness is eating. [new 2015]

Enable adults with type 1 diabetes who are hospital inpatients to self-administer subcutaneous insulin if they are willing and able and it is safe to do so. [new 2015]

Delivery of Care

From the time of admission, the adult with type 1 diabetes and the team caring for him or her should receive, on a continuing basis, advice from a trained multidisciplinary team with expertise in diabetes. [2004]

Throughout the course of an inpatient admission, respect the personal expertise of adults with type 1 diabetes (in managing their own diabetes) and routinely integrate this into ward-based blood glucose monitoring and insulin delivery. [2004, amended 2015]

Throughout the course of an inpatient admission, the personal knowledge and needs of adults with type 1 diabetes regarding their dietary requirements should be a major determinant of the food choices offered to them, except when illness or medical or surgical intervention significantly disturbs those requirements. [2004]

Members of care teams caring for adults with type 1 diabetes in institutions, such as nursing homes, residential homes and prisons, should follow the recommendations in this section. [2004]

Provide optimal insulin therapy, which can be achieved by the use of intravenous insulin and glucose, to all adults with type 1 diabetes with threatened or actual stroke. Critical care and emergency departments should have a protocol for such management. [2004, amended 2011]

Managing Complications

Eye Disease

On diagnosis, GPs should immediately refer adults with type 1 diabetes to the local eye screening service. Perform screening as soon as possible and no later than 3 months from referral. Arrange repeat structured eye screening annually. [2004, amended 2016]

Depending on the findings, follow structured eye screening by:

- Routine review annually or
- Earlier review or
- Referral to an ophthalmologist [2004, amended 2015]

Explain the reasons and success of eye screening systems to adults with type 1 diabetes, so that attendance is not reduced by lack of knowledge or fear of outcome. [2004]

Offer digital retinopathy screening annually to adults with type 1 diabetes. [2004, amended 2015]

Use mydriasis with tropicamide when photographing the retina, after prior agreement with the adult with type 1 diabetes after discussion of the advantages and disadvantages, including appropriate precautions for driving. [2004]

Make visual acuity testing a routine part of eye screening programmes. [2004, amended 2015]

Ensure that emergency review by an ophthalmologist occurs for:

- Sudden loss of vision
- Rubeosis iridis
- Pre-retinal or vitreous haemorrhage
- Retinal detachment [2004, amended 2015]

Ensure that rapid review by an ophthalmologist occurs for new vessel formation. [2004, amended 2015]

Refer to an ophthalmologist for:

- Referable maculopathy:
    - Exudate or retinal thickening within 1 disc diameter of the centre of the fovea
    - Circinate or group of exudates within the macula (the macula is defined here as a circle centred on the fovea, of a diameter the distance between the temporal border of the optic disc and the fovea)
    - Any microaneurysm or haemorrhage within 1 disc diameter of the centre of the fovea, only if associated with a best visual acuity of 6/12 or worse
- Referable pre-proliferative retinopathy:
    - Any venous beading
    - Any venous reduplication

- Any intraretinal microvascular abnormalities (IRMA)
- Multiple deep, round or blot haemorrhages
  (If cotton wool spots are present, look carefully for the above features, but cotton wool spots themselves do not define pre proliferative retinopathy)

- Any large sudden unexplained drop in visual acuity [2004, amended 2015]

Diabetic Kidney Disease

For guidance on managing kidney disease in adults with type 1 diabetes, see the NGC summary of the NICE guideline Chronic kidney disease. Early identification and management of chronic kidney disease in adults in primary and secondary care. [new 2015]

Ask all adults with type 1 diabetes with or without detected nephropathy to bring in the first urine sample of the day ('early morning urine') once a year. Send this for estimation of albumin:creatinine ratio. Estimation of urine albumin concentration alone is a poor alternative. Serum creatinine should be measured at the same time. [2004]

Suspect other renal disease:

- In the absence of progressive retinopathy
- If blood pressure is particularly high
- If proteinuria develops suddenly
- If significant haematuria is present
- In the presence of systemic ill health [2004]

Discuss the significance of a finding of albuminuria with the person concerned. [2004, amended 2015]

Start angiotensin-converting enzyme (ACE) inhibitors and, with the usual precautions, titrate to full dose in all adults with confirmed nephropathy (including those with moderately increased albuminuria ['microalbuminuria'] alone) and type 1 diabetes. [2004, amended 2015]

If ACE inhibitors are not tolerated, substitute angiotensin 2 receptor antagonists. Combination therapy is not recommended. [2004, amended 2015]

Maintain blood pressure below 130/80 mmHg by addition of other anti-hypertensive drugs if necessary. [2004]

Advise adults with type 1 diabetes and nephropathy about the advantages of not following a high-protein diet. [2004]

Referral criteria for tertiary care should be agreed between local diabetes specialists and nephrologists. [2004]

Chronic Painful Diabetic Neuropathy

For guidance on managing chronic painful diabetic neuropathy in adults with type 1 diabetes, see the NGC summary of the NICE guideline Neuropathic pain - pharmacological management. The pharmacological management of neuropathic pain in adults in non-specialist settings. [new 2015]

Autonomic Neuropathy

In adults with type 1 diabetes who have unexplained diarrhoea, particularly at night, the possibility of autonomic neuropathy affecting the gut should be considered. [2004]

Take care when prescribing antihypertensive medicines not to expose people to the risks of orthostatic hypotension as a result of the combined effects of sympathetic autonomic neuropathy and blood pressure lowering medicines. [2004]

In adults with type 1 diabetes who have bladder emptying problems, investigate the possibility of autonomic neuropathy affecting the bladder, unless other explanations are adequate. [2004]

When managing the symptoms of autonomic neuropathy, include standard interventions for the manifestations encountered (for example, for abnormal sweating and postural hypotension). [2004, amended 2015]

Anaesthetists should be aware of the possibility of parasympathetic autonomic neuropathy affecting the heart in adults with type 1 diabetes who are listed for procedures under general anaesthetic and who have evidence of somatic neuropathy or other manifestations of autonomic neuropathy. [2004]

Gastroparesis

Advise a small-particle-size diet (mashed or pureed food) for symptomatic relief for adults with type 1 diabetes who have vomiting caused by gastroparesis[1]. [new 2015]

Consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy for adults with type 1 diabetes who have gastroparesis. [new 2015]

For adults with type 1 diabetes who have vomiting caused by gastroparesis, explain that:

- There is no strong evidence that any available antiemetic therapy is effective
- Some people have had benefit with domperidone[2], erythromycin[3] or metoclopramide[4]
- The strongest evidence for effectiveness is for domperidone[2], but prescribers must take into account its safety profile, in particular its cardiac risk and potential interactions with other medicines [new 2015]

For treating vomiting caused by gastroparesis in adults with type 1 diabetes:

- Consider alternating use of erythromycin[3] and metoclopramide[4]
- Consider domperidone[2] only in exceptional circumstances (that is, when it is the only effective treatment) and in accordance with Medicines and Healthcare Products Regulatory Agency (MHRA) guidance [new 2015]

Refer adults with type 1 diabetes who have gastroparesis for specialist advice if the interventions in the recommendations above are not beneficial or not appropriate. [new 2015]

Acute Painful Neuropathy of Rapid Improvement of Blood Glucose Control

Reassure adults with type 1 diabetes that acute painful neuropathy resulting from rapid improvement of blood glucose control is a self-limiting condition that improves symptomatically over time. [new 2015]

Explain to adults with type 1 diabetes that the specific treatments for acute painful neuropathy resulting from rapid improvement of blood glucose control:

- Have the aim of making the symptoms tolerable until the condition resolves
- May not relieve pain immediately and may need to be taken regularly for several weeks to be effective [new 2015]

Use of simple analgesics (paracetamol, aspirin) and local measures (bed cradles) are recommended as a first step, but if trials of these measures are ineffective, discontinue them and try other measures. [2004]

Do not relax diabetes control to address acute painful neuropathy resulting from rapid improvement of blood glucose control in adults with type 1 diabetes. [new 2015]

If simple analgesia does not provide sufficient pain relief for adults with type 1 diabetes who have acute painful neuropathy resulting from rapid improvement of blood glucose control, offer treatment as described in the NGC summary of the NICE guideline Neuropathic pain - pharmacological management. The pharmacological management of neuropathic pain in adults in non-specialist settings. Simple analgesia may be continued until the effects of additional treatments have been established. [new 2015]

When offering medicines for managing acute painful neuropathy resulting from rapid improvement of blood glucose control to adults with type 1 diabetes, be aware of the risk of dependency associated with opioids. [new 2015]

Diabetic Foot Problems

For guidance on preventing and managing foot problems in adults with type 1 diabetes, see the NGC summary of the NICE guideline Diabetic foot problems: prevention and management. [new 2015]

Erectile Dysfunction

Offer men with type 1 diabetes the opportunity to discuss erectile dysfunction as part of their regular review. [new 2015]

Offer a phosphodiesterase-5 inhibitor to men with type 1 diabetes with isolated erectile dysfunction unless contraindicated. Choose the phosphodiesterase-5 inhibitor with the lowest acquisition cost. [new 2015]

Consider referring men with type 1 diabetes to a service offering further assessment and other medical, surgical or psychological management of erectile dysfunction if phosphodiesterase-5 inhibitor treatment is unsuccessful or contraindicated. [new 2015]

Thyroid Disease Monitoring

Measure blood thyroid-stimulating hormone (TSH) levels in adults with type 1 diabetes at annual review. [new 2015]

Psychological Problems

Members of diabetes professional teams providing care or advice to adults with type 1 diabetes should be alert to the development or presence of clinical or subclinical depression and/or anxiety, in particular if someone reports or appears to be having difficulties with self-management. [2004]

Diabetes professionals should:

- Ensure that they have appropriate skills in the detection and basic management of non-severe psychological disorders in people from different cultural backgrounds
- Be familiar with appropriate counselling techniques and drug therapy, while arranging prompt referral to specialists of those people in whom psychological difficulties continue to interfere significantly with wellbeing or diabetes self-management

See also the NGC summaries of the NICE guidelines Common mental health disorders. Identification and pathways to care and Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. Management in primary, secondary and community care, and the NICE guideline Depression in adults with a chronic physical health problem. [2004, amended 2015]

Eating Disorders

Members of diabetes professional teams should be alert to the possibility of bulimia nervosa, anorexia nervosa and insulin dose manipulation in adults with type 1 diabetes with:

- Over-concern with body shape and weight
- Low BMI
- Hypoglycaemia
- Suboptimal overall blood glucose control

See also the NICE guideline on eating disorders. [2004, amended 2015]

The risk of morbidity from the complications of poor metabolic control suggests that consideration should be given to early, and occasionally urgent, referral of adults with type 1 diabetes to local eating disorder services. [2004]

Make provision for high-quality professional team support at regular intervals with regard to counselling about lifestyle issues and particularly dietary behaviour for all adults with type 1 diabetes from the time of diagnosis (see sections above). [2004]

Footnotes

[1]Diagnosis of gastroparesis needing specific therapy can only be made in the absence of hyperglycaemia at the time of testing, because hyperglycaemia induces a physiological delay in gastric emptying.

[2]MHRA guidance (2014) notes that domperidone is associated with a small increased risk of serious cardiac side effects. Domperidone is now contraindicated in certain groups in whom the risk of cardiac effects is higher; its marketing authorisations have also been restricted to its use in the relief of nausea and vomiting only, at the lowest effective dose and for the shortest possible time (usually not more than 1 week): see the MHRA guidance and summaries of product characteristics. The MHRA advises that prescribers should take into account the overall safety profile of domperidone, and in particular its cardiac risk and potential interactions with other medicines (such as erythromycin), if there is a clinical need to use it at doses or durations greater than those authorised. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[3]At the time of publication (August 2015), erythromycin did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. NICE has published an evidence summary: unlicensed or off-label medicine on oral erythromycin for gastroparesis in adults, including a version

for the public.

[4]MHRA guidance (2013) notes that metoclopramide has well-known risks of neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia. It advises that metoclopramide should be prescribed only for short-term use (up to 5 days) at a maximum dose of 30 mg in 24 hours (usual dose of 10 mg up to 3 times a day).

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when it is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation Wording in Guideline Updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of The guidelines manual (January 2009). This does not apply to any recommendations ending [2004]. In particular, for recommendations labelled [2004] and [2004, amended 2015] the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) care pathway titled "Type 1 diabetes in adults overview" is available from the NICE Web site.

The following algorithms are provided in the full version of the guideline (see the "Availability of Companion Documents" field):

- Blood glucose monitoring: frequency, timing and targets
- Treatment
- Non-glycaemic management of CV risk factors

Scope

Disease/Condition(s)

Type 1 diabetes and its complications and associated conditions, especially eye, kidney, and nerve damage and arterial disease affecting the heart, brain, and feet

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Nutrition

Psychology

Intended Users

Advanced Practice Nurses

Dietitians

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Optometrists

Patients

Pharmacists

Physicians

Podiatrists

Psychologists/Non-physician Behavioral Health Clinicians

Public Health Departments

Social Workers

Guideline Objective(s)

- To provide evidence-based, practical advice on supporting adults with type 1 diabetes to live full, largely unrestricted, lives and to avoid the

short-term and long-term complications of both the disease and of its treatment
- To describe methods for achieving optimal outcomes for adults with type 1 diabetes and to inform service design and delivery

Target Population

Adults (aged 18 years or older) with type 1 diabetes

Interventions and Practices Considered

Diagnosis/Evaluation

1. Recognizing type 1 diabetes in adults with hyperglycaemia
2. Measurement of autoantibodies (not recommended routinely)
3. Measurement of C-peptide (not recommended routinely)
4. Medical assessment
5. Environmental assessment
6. Cultural and education assessment
7. Assessment of emotional state
8. Development of an early care plan based on assessments

Management/Treatment/Prevention

1. Provision of open-access services
2. Individual care plan to be reviewed annually that includes the following:
    - Diabetes education including nutritional advice
    - Insulin therapy
    - Self monitoring
    - Avoiding hypoglycaemia and maintaining awareness of hypoglycaemia
    - For women of childbearing potential, family planning, contraception and pregnancy planning
    - Cardiovascular risk factor monitoring and management
    - Complications monitoring and management
    - Means and frequency of communicating with the diabetes professional team
    - Frequency and content of follow-up consultations, including review of glycated haemoglobin (HbA1c) levels and experience of hypoglycaemia, and next annual review
3. Multidisciplinary team approach to in-patients with diabetes
4. Structured education and information (e.g., the DAFNE [dose-adjustment for normal eating] programme)
5. Dietary management
    - Carbohydrate counting
    - Low glycaemic index diet (not recommended)
    - Dietary advice
6. Advice on physical activity
7. Blood glucose management
    - HbA1c measurement and targets
    - Self-monitoring of blood glucose
    - Continuous glucose monitoring (not recommended routinely)
8. Insulin therapy
    - Insulin regimens
    - Use of long-acting insulin
    - Continuous subcutaneous insulin infusion (CSII or insulin pump) therapy
    - Rapid-acting insulin analogues
    - Mixed insulin
    - Optimising insulin therapy
    - Adding metformin to insulin therapy
    - Insulin delivery (injection devices and needle choice, injection sites)

9. Referral for islet or pancreas transplantation
10. Awareness, management, and prevention of hypoglycaemia
11. Ketone monitoring and management of diabetic ketoacidosis
12. Recognising associated autoimmune disease (e.g., coeliac disease, Addison's disease, pernicious anaemia, thyroid disease)
13. Control of cardiovascular risk
    - Aspirin (not recommended for primary prevention)
    - Assessing cardiovascular risk factors
    - Interventions to reduce risk and manage cardiovascular disease
    - Blood pressure management
14. Care of adults with type 1 diabetes in hospital
    - Blood glucose control
    - Delivery of care
15. Managing/preventing diabetic complications (eye disease, diabetic kidney disease, painful diabetic neuropathy, gastroparesis, autonomic neuropathy, diabetic foot problems, thyroid disease monitoring, erectile dysfunction, psychological problems, eating disorders)

Major Outcomes Considered

- Health-related quality of life
- Adverse events and complications
- Mortality
- Glycated haemoglobin (HbA1c) levels
- Hypoglycaemia

Note: The outcomes listed above are the "main outcomes" considered. See Table 1 in the full version of the guideline (see the "Availability of Companion Documents" field) for a complete list of outcomes considered for each of the review questions.

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC), which is based at the Royal College of Physicians, on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing the Review Questions and Outcomes

Review questions were developed in a patient, intervention, comparison and outcome (PICO) framework for intervention reviews, and an adapted PICO framework was used for other types of review (such as diagnosis).

This use of a framework guided the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations by the Guideline Development Group (GDG). The review questions were drafted by the National Clinical Guideline Centre (NCGC) technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (see Appendix A in the full guideline appendices [see the "Availability of Companion Documents" field]). A total of 29 review questions were identified. Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Searching for Evidence

Clinical Literature Search

Systematic literature searches were undertaken to identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within The guidelines manual 2012 (see the "Availability of Companion Documents" field). Databases were searched using relevant medical subject headings, free-text terms and study design filters where appropriate. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. All searches were conducted in Medline, EMBASE and The Cochrane Library. All searches were updated on August 28, 2014. No papers published after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GDG members to highlight any additional studies. The questions, the study types applied, the databases searched and the dates covered can be found in Appendix F of the full version of the guideline.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were assessed against the inclusion criteria.

During the scoping stage, a search was conducted for guidelines and reports on the Web sites listed below and on those of organisations relevant to the topic. Searching for grey literature or unpublished literature was not undertaken. All references sent by stakeholders were considered.

- Guidelines International Network database (www.g-i-n.net)
- National Guideline Clearinghouse (NGC) (www.guideline.gov)
- National Institute for Health and Care Excellence (NICE) (www.nice.org.uk)
- NICE Evidence Search (www.evidence.nhs.uk)

Health Economic Literature Search

Systematic literature searches were also undertaken to identify health economic evidence within published literature relevant to the review questions. The evidence was identified by conducting a broad search relating to type 1 diabetes in the National Health Service Economic Evaluation Database (NHS EED), the Health Technology Assessment database (HTA) and the Health Economic Evaluations Database (HEED) with no date restrictions. Additionally, the search was run on Medline and EMBASE using an economic filter, from 2009, to ensure recent publications that had not yet been indexed by the economic databases were identified. Studies published in languages other than English were not reviewed. Where possible, searches were restricted to articles published in English. The health economic search strategies are included in Appendix F of the full version of the guideline document. All searches were updated on August 28, 2014. No papers published after this date were considered.

Evidence of Effectiveness

The evidence was reviewed following these steps:

- Potentially relevant studies were identified for each review question from the search results by reviewing titles and abstracts. Full papers were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review question in the appropriate population (review protocols are included in Appendix C in the full guideline appendices).

Inclusion and Exclusion Criteria

The inclusion and exclusion of studies was based on the review protocols, which can be found in Appendix C in the full guideline appendices. Excluded studies by review question (with the reasons for their exclusion) are listed in Appendix K in the full guideline appendices. The GDG was consulted about any uncertainty regarding inclusion or exclusion.

Randomised trials, non-randomised trials, and observational studies were included in the evidence reviews as appropriate. Literature reviews, posters, letters, editorials, comment articles, unpublished studies, conference abstracts (unless stated in cases where there was limited evidence) and studies not in English were excluded.

The review protocols are presented in Appendix C in the full guideline appendices.

Evidence of Cost-effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their 'cost-effectiveness') rather

than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature
- Undertook new cost-effectiveness analysis in priority areas

Literature Review

The health economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts. Full papers were then obtained.
- Reviewed full papers against prespecified inclusion and exclusion criteria to identify relevant studies.

Inclusion and Exclusion Criteria

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost-effectiveness, cost–benefit and cost–consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially includable as economic evidence.

Studies that only reported cost per hospital (not per patient), or only reported average cost-effectiveness without disaggregated costs and effects, were excluded. Literature reviews, abstracts, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available, then other less relevant studies may not have been included. Where selective exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (Appendix E of The guidelines manual and the health economics review protocol in Appendix C in the full guideline appendices).

When no relevant economic studies were found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implications of the recommendations.

Number of Source Documents

See Appendix D in the full guideline appendices (see the "Availability of Companion Documents" field) for a flow chart for clinical article selection for each topic considered in the 2015 guideline update.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC), which is based at the Royal College of Physicians, on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Evidence of Effectiveness

The evidence was reviewed following these steps:

- Relevant studies were critically appraised using the appropriate checklist as specified in The guidelines manual (see the "Availability of Companion Documents" field).
- Key information was extracted on the study's methods, PICO (Population, Intervention, Comparator, Outcome) factors and results. These were presented in summary tables (in each review chapter) and evidence tables (in Appendix G in the full guideline appendices [see the "Availability of Companion Documents" field]).
- Summaries of evidence were generated by outcome (included in the relevant review chapters) and were presented in Guideline Development Group (GDG) meetings:
    - Randomised studies: data were meta-analysed where appropriate and reported in GRADE (Grading of Recommendations Assessment, Development and Evaluation) profiles (for intervention reviews).
    - Observational studies – comparative studies: data were presented narratively or results were tabulated, and reported in GRADE profiles (for intervention reviews).
    - Observational studies – non-comparative studies: data were presented narratively or results were tabulated.

Methods of Combining Clinical Studies

Data Synthesis for Intervention Reviews

Where possible, meta-analyses were conducted to combine the results of studies for each review question using Cochrane Review Manager (RevMan5) software. Fixed-effects (Mantel-Haenszel) techniques were used to calculate risk ratios (relative risk) for binary outcomes.

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation) were required for meta-analysis. Data for continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences. However, in cases where standard deviations were not reported per intervention group, the standard error (SE) for the mean difference was calculated from other reported statistics (*p* values or 95% confidence intervals [CIs]); meta-analysis was then undertaken for the mean difference and SE using the generic inverse variance method in RevMan5. When the only evidence was based on studies that summarised results by presenting medians (and interquartile ranges), or only *p* values were given, this information was reported narratively and generally included in the GRADE tables without calculating the relative or absolute effects. Consequently, aspects of quality assessment such as imprecision of effect could not be assessed for evidence of this type. Where reported, and possible to calculate, time-to-event data was presented as a hazard ratio (HR).

Where *p* values were used as part of calculations for continuous outcomes, if a *p* value was reported as 'less than', a conservative approach was undertaken. For example, if *p* value was reported as '$p \leq 0.001$', the calculations for standard deviations will be based on a *p* value of 0.001. If these statistical measures were not available then data were reported narratively.

Statistical heterogeneity was assessed by visually examining the forest plots, and by considering the chi-squared test for significance at $p<0.1$ or an I-squared inconsistency statistic (with an I-squared value of more than 50% indicating considerable heterogeneity).

For interpretation of the binary outcome results, differences in the absolute event rate were calculated using the GRADEpro software, for the median event rate across the control arms of the individual studies in the meta-analysis. Absolute risk differences (ARDs) were presented in the GRADE profiles and in clinical summary of findings tables, for discussion with the GDG. For binary outcomes, absolute event rates were also calculated using the GRADEpro software using event rate in the control arm of the pooled results.

An network meta-analysis (NMA) was conducted for the review on long-acting insulin. This type of analysis simultaneously compares multiple treatments in a single meta-analysis, preserving the randomisation of randomised controlled trials (RCTs) included in the reviews of direct comparisons trials. The aim of the NMA was to include all relevant evidence in order both to answer questions on the clinical effectiveness of interventions when no direct comparison was available and to give a ranking of treatments in terms of efficacy. The output was expressed as mean and Bayesian 95% credible intervals (CrIs) for the rank of each long-acting insulin regimen and as mean effect estimates and their Bayesian 95% CrIs for each of the included outcomes.

A Bayesian NMA was performed using the software WinBUGS version 1.4.3. That allowed inclusion of multi-arm trials and accounts for the correlation between arms in the trials with any number of trial arms.

The following were the main outputs from the NMA:

- Rate ratios of severe/major hypoglycaemic events (with their 95% CrIs) calculated using direct and indirect evidence
- Changes in glycated haemoglobin (HbA1c) level (with their 95% CrIs) calculated using direct and indirect evidence
- A ranking of long-acting insulin regimens compared with insulin NPH (twice daily) (with 95% CrIs for the ranks) for each network.

A full technical account can be found in Appendix M in the full guideline appendices.

Appraising the Quality of Evidence by Outcomes

The evidence for outcomes from the included RCTs and, where appropriate, comparative observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking into account individual study quality factors and the meta-analysis results. Results were presented in GRADE profiles ('GRADE tables'), which consist of 2 sections: the 'Clinical evidence profile' table includes details of the quality assessment while the 'Clinical evidence summary of findings' table includes pooled outcome data, where appropriate, an absolute measure of intervention effect and the summary of quality of evidence for that outcome. In this table, the columns for intervention and control indicate summary measures and measures of dispersion (such as mean and standard deviation or median and range) for continuous outcomes and frequency of events (n/N: the sum across studies of the number of patients with events divided by sum of the number of completers) for binary outcomes. Reporting or publication bias was taken into consideration in the quality assessment and only included in the 'Clinical evidence profile' table if it was apparent from GDG members.

The evidence for each outcome was examined separately for the quality elements listed and defined in Table 2 in the full version of the guideline. Each element was graded using the quality levels listed in Table 3 in the full version of the guideline. The main criteria considered in the rating of these elements are discussed below. Footnotes were used to describe reasons for grading a quality element as having serious or very serious problems. The ratings for each component were summed to obtain an overall assessment for each outcome (see the "Rating Scheme for the Strength of the Evidence" field).

The GRADE toolbox is currently designed only for randomised trials and comparative observational studies, for non-comparative observational studies, the results, study limitations and overall quality assessment ratings were reported narratively.

Grading the Quality of Clinical Evidence: RCTs and Comparative Observational Studies

After results were pooled, the overall quality of evidence for each outcome was considered. The following procedure was adopted when using GRADE:

1. A quality rating was assigned, based on the study design. RCTs start as High, observational cohort studies as Low.
2. The rating was then downgraded for the specified criteria: risk of bias (study limitations), inconsistency, indirectness, imprecision and publication bias. These criteria are detailed in Sections 3.3.7 to 3.3.10 of the full version of the guideline. Evidence from observational cohort studies (which had not previously been downgraded) was upgraded if there was: a large magnitude of effect, a dose–response gradient, and if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect. Each quality element considered to have 'serious' or 'very serious' risk of bias was rated down by 1 or 2 points respectively.
3. The downgraded or upgraded marks were then summed and the overall quality rating was revised. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if 1, 2 or 3 points were deducted respectively.
4. The reasons or criteria used for downgrading were specified in the footnotes.

Grading the Quality of Clinical Evidence: Non-comparative Observational Studies

A customised quality assessment checklist (adapted from the NICE prognostic studies checklist) has been used for assessing the quality of non-

comparative observational studies (for example, cross-sectional studies or case-series), and so for reviews that included these study types, the main criteria considered in assessing study quality were:

- The study design: if it is retrospective or prospective, or cross-sectional. Retrospective studies are more likely to be at higher risk of bias.
- The study sample is representative of the population of interest with regard to key characteristics, sufficient to limit potential bias to the results
- The outcome of interest is adequately measured in study participants, sufficient to limit bias
- Important potential confounders are appropriately accounted for in the statistical analysis, limiting potential bias with respect to the outcomes of interest, and the presentation of invalid results

All non-comparative observational studies were graded as Low quality due to the inherent high risk of bias associated with these study designs. However, the specific methodological limitations of the studies included in the guideline update, have been summarised in tables within Appendix I of the full version of the guideline, in order to give an overview of the quality of each individual study. As GRADE is currently not designed for these types of studies, quality has been assessed by study only, rather than by outcome in the review. Raw data, or odds ratios, relative risks or hazard ratios, with their 95% CIs, from multivariate analyses were extracted from the papers where appropriate to the review question. Data for the outcomes defined in the review protocols has been summarised in tables within the relevant review chapter. Full data for all the outcomes has been reported in the evidence tables (see Appendix G of the full guideline appendices) for each individual observational study.

Assessing Clinical Importance

The GDG assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into ARDs using GRADEpro software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

The assessment of benefit, harm, or no benefit or harm was based on the point estimate of absolute effect for intervention studies. This assessment was carried out by the GDG for each outcome, and an evidence summary table was produced to compile the GDG's assessments of clinical importance per outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

Evidence Statements

Evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty or uncertainty in the estimate of effect. The evidence statements encompass the following key features of the evidence:

- The intervention and comparison group under investigation
- The outcome measure being assessed
- An indication of the direction of effect (if one treatment is beneficial or harmful compared with the other, or whether there is no difference between the 2 tested treatments). Determination of benefit, harm, or no difference, is based on the GDG's interpretation of whether the absolute effect could be considered clinically beneficial, clinically harmful, or no clinical effect or difference between the intervention and comparison groups
- The time-point the outcomes have been assessed at
- A description of the overall quality of evidence (GRADE overall quality)

Evidence of Cost-effectiveness

The GDG is required to make decisions based on the best available evidence of both clinical and cost effectiveness. Guideline recommendations should be based on the expected costs of the different options in relation to their expected health benefits (that is, their 'cost-effectiveness') rather than the total implementation cost. Thus, if the evidence suggests that a strategy provides significant health benefits at an acceptable cost per patient treated, it should be recommended even if it would be expensive to implement across the whole population.

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the published economic literature
- Undertook new cost-effectiveness analysis in priority areas

Literature Review

The health economist:

- Critically appraised relevant studies using the economic evaluations checklist as specified in The guidelines manual.

- Extracted key information about the studies; methods and results into evidence tables (included in Appendix H in the full guideline appendices).
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter for each review question) – see below for details.

NICE Economic Evidence Profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows an assessment of applicability and methodological quality for each economic evaluation, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The guidelines manual. It also shows the incremental costs, incremental effects (for example, quality-adjusted life years [QALYs]) and incremental cost-effectiveness ratio for the base case analysis in the evaluation, as well as information about the assessment of uncertainty in the analysis. See Table 6 in the full version of the guideline for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity.

Methods Used to Formulate the Recommendations

Expert Consensus

Expert Consensus (Nominal Group Technique)

Informal Consensus

Description of Methods Used to Formulate the Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Clinical Guideline Centre (NCGC), which is based at the Royal College of Physicians, on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Who Developed This Guideline

The Guideline Development Group (GDG) was convened by the NCGC and chaired in accordance with guidance from NICE.

The group met every 6 weeks during the development of the guideline. Staff from the NCGC provided methodological support and guidance for the development process. The team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. They undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate and drafted the guideline in collaboration with the GDG.

Developing Recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendices G and H in the full guideline appendices (see the "Availability of Companion Documents" field).
- Summaries of clinical and economic evidence and quality (as presented in Chapters 6 to 16 of the full version of the guideline).
- Forest plots and summary receiver-operating characteristic (ROC) curves (Appendix J in the full guideline appendices).
- A description of the methods and results of the cost-effectiveness analysis(ses) undertaken for the guideline (Appendices N to P in the full guideline appendices).

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. This was either done formally in an economic model, or informally. Firstly, the net benefit over harm (clinical effectiveness) was considered, focusing on the critical outcomes. When this was done informally, the GDG took into account the clinical benefits and harms when one intervention was compared with another. The assessment of net benefit was moderated by the importance placed on the outcomes (the GDG's values and preferences), and the confidence the GDG had in the evidence (evidence quality). Secondly, it was assessed whether the net benefit justified any differences in costs.

When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion.

The considerations for making consensus-based recommendations include the balance between potential harms and benefits, the economic costs compared with the economic benefits, current practices, and recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were agreed through discussions in the GDG. The GDG considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (see Appendix R in the full guideline appendices).

The wording of recommendations was agreed by the GDG and focused on the following factors:

- The actions health professionals need to take
- The information readers need to know
- The strength of the recommendation (for example the word 'offer' was used for strong recommendations and 'consider' for weak recommendations)
- The involvement of patients (and their carers if needed) in decisions on treatment and care
- Consistency with NICE's standard advice on recommendations about drugs, waiting times and ineffective interventions

The main considerations specific to each recommendation are outlined in the 'recommendations and link to evidence' sections within each chapter of the full version of the guideline.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GDG uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GDG uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation Wording in Guideline Updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of The guidelines manual (January 2009). This does not apply to any recommendations ending [2004]. In particular, for recommendations labelled [2004] and [2004, amended 2015] the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Cost Analysis

Undertaking New Health Economic Analysis

As well as reviewing the published economic literature for each review question, new economic analysis was undertaken by the health economist in selected areas. Priority areas for new health economic analysis were agreed by the Guideline Development Group (GDG) after formation of the review questions and consideration of the available health economic evidence.

The following general principles were adhered to in developing the cost-effectiveness analysis:

- Methods were consistent with the National Institute for Health and Care Excellence (NICE) reference case.
- The GDG was involved in the design of the model, selection of inputs and interpretation of the results.
- Model inputs were based on the systematic review of the clinical literature supplemented with other published data sources where possible.
- When published data was not available GDG expert opinion was used to populate the model.
- Model inputs and assumptions were reported fully and transparently.
- The results were subject to sensitivity analysis and limitations were discussed.
- The model was peer-reviewed by another health economist at the National Clinical Guideline Centre (NCGC).

Full methods for the cost-effectiveness analyses conducted for this guideline are described in Appendix N, O and P in the full the guideline appendices (see the "Availability of Companion Documents" field).

Cost-effectiveness Criteria

The NICE report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies)
- The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'Recommendations and link to evidence' section of the relevant chapter in the full version of the guideline, with reference to issues regarding the plausibility of the estimate or to the factors set out in 'Social value judgements: principles for the development of NICE guidance'.

Full methods for the cost-effectiveness analyses conducted for the guideline are described in Appendix N, O and P in the full guideline appendices.

In the Absence of Economic Evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost-effectiveness by considering expected differences in resource use between options and relevant UK National Health Service (NHS) unit costs, alongside the results of the clinical review of effectiveness evidence. The UK NHS costs reported in the guideline were those presented to the GDG and they were correct at the time recommendations were drafted; they may have been revised subsequently by the time of publication. However, the GDG has no reason to believe they have been changed substantially.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Validation Process

This guidance is subject to a 12 week public consultation and feedback as part of the quality assurance and peer review of the document. All comments received from registered stakeholders are responded to in turn and posted on the National Institute for Health and Care Excellence (NICE) Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. If the Guideline Development Group (GDG) believed RCT data were not appropriate or there was limited evidence from RCTs, well-conducted non-randomised studies were included. Please refer to Appendix C of the full guideline appendices (see the "Availability of Companion Documents" field) for full details on the study design of studies selected for each review question. It was considered unlikely that the search would find any RCTs.

Where data from observational studies were included, the GDG decided that the results for each outcome should be presented separately for each study and meta-analysis was not conducted

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

These guideline recommendations aim to help healthcare professionals in all settings encourage and support optimum lifestyle choices and self-management strategies among patients. An accurate diagnosis by the healthcare professional is key if the patient is to receive the relevant therapies. Rigorous control of blood glucose from the point of diagnosis onwards will yield benefits for the rest of the patient's life. Structured education programmes are an important mechanism for helping the patient understand and embrace the behavioural changes that will secure these benefits.

Refer to the "Trade-off between clinical benefits and harms" sections in the full version of the guideline for (see the "Availability of Companion Documents" field) for details about benefits of specific interventions.

Potential Harms

- Providing a blood sample may cause distress to some children and occasionally to adults.
- Misinterpretation of a test, for example, negative antibody testing and/or detection of C-peptide, may lead to misclassification of diabetes as not being type 1, and lead to the mistaken withdrawal of insulin therapy.
- Adverse effects of insulin therapy, including hypoglycaemia and injection site reactions
- Side-effects associated with adjunct therapy administration can include gastrointestinal side-effects, nausea, vomiting and anorexia for the agents.
- The risks of transplantation include those of the surgeries themselves, and also the potential side-effects of the immunosuppressive medications that need to be taken after transplant. Additionally, long-term insulin independence is difficult to maintain.
- Adverse effects of angiotensin-converting enzyme (ACE) inhibitors described in clinical trials and found to be problematic in clinical use include a persistent cough.
- The use of phosphodiesterase-5 inhibitors (PDEIs) was associated with a significantly increased risk of developing adverse events when compared with placebo. Adverse events included headaches, flushing, upper respiratory tract infections, dyspepsia and abnormal vision.

Refer to the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for details about harms of specific interventions.

Contraindications

Contraindications

- See Section 10.3 (Clinical Evidence) regarding pancreas transplantation in the full version of the guideline for contraindications to immunosuppressants and surgery.
- American Diabetes Association guidelines indicate that meta-analysis and large-scale collaborative trials in men and women with diabetes support the view that low-dose aspirin therapy should be prescribed as a secondary prevention strategy if no contraindications exist. Contraindications reported include allergy, bleeding tendency, anticoagulant therapy, recent gastrointestinal bleeding and clinically active hepatic disease.

- The indications and contraindications for thrombolysis in patients with diabetes are the same as those without.
- Contraindications to phosphodiesterase-5 inhibitors listed by the British National Formulary include concomitant use of nitrates, where vasodilation or sexual activity is inadvisable, men with a history of non-arteritic anterior ischaemic optic neuropathy; to which manufacturers have added systolic blood pressure below 90 mmHg, recent stroke, unstable angina, and myocardial infarction.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.
- This guideline recommends some medicines for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information. Where recommendations have been made for the use of medicines outside their licensed indications ('off-label use'), these medicines are marked with a footnote in the recommendations.
- See the "Person-centred care" section in the original guideline document for information about individual needs and preferences and transition of care.

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help users put the guideline into practice are available (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Education and Information

Offer all adults with type 1 diabetes a structured education programme of proven benefit, for example the DAFNE (dose-adjustment for normal eating) programme. Offer this programme 6 to 12 months after diagnosis. [new 2015]

Blood Glucose Management

Support adults with type 1 diabetes to aim for a target glycated haemoglobin (HbA1c) level of 48 mmol/mol (6.5%) or lower, to minimise the risk of long-term vascular complications. [new 2015]

Agree an individualised HbA1c target with each adult with type 1 diabetes, taking into account factors such as the person's daily activities, aspirations, likelihood of complications, comorbidities, occupation and history of hypoglycaemia. [new 2015]

Support adults with type 1 diabetes to test at least 4 times a day, and up to 10 times a day if any of the following apply:

- The desired target for blood glucose control, measured by HbA1c level, is not achieved
- The frequency of hypoglycaemic episodes increases
- There is a legal requirement to do so (such as before driving, in line with the Driver and Vehicle Licensing Agency [DVLA] At a glance guide to the current medical standards of fitness to drive)
- During periods of illness
- Before, during and after sport
- When planning pregnancy, during pregnancy and while breastfeeding (see the see the NGC summary of the NICE guideline Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period)
- If there is a need to know blood glucose levels more than 4 times a day for other reasons (for example, impaired awareness of hypoglycaemia, high-risk activities) [new 2015]

Advise adults with type 1 diabetes to aim for:

- A fasting plasma glucose level of 5 mmol/litre to 7 mmol/litre on waking and
- A plasma glucose level of 4 mmol/litre to 7 mmol/litre before meals at other times of the day [new 2015]

Insulin Therapy

Offer multiple daily injection basal–bolus insulin regimens, rather than twice-daily mixed insulin regimens, as the insulin injection regimen of choice for all adults with type 1 diabetes. Provide the person with guidance on using multiple daily injection basal–bolus insulin regimens. [new 2015]

Awareness and Management of Hypoglycaemia

Assess awareness of hypoglycaemia in adults with type 1 diabetes at each annual review. [new 2015]

Care of Adults with Type 1 Diabetes in Hospital

Enable adults with type 1 diabetes who are hospital inpatients to self-administer subcutaneous insulin if they are willing and able and it is safe to do so. [new 2015]

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Clinical Guideline Centre. Type 1 diabetes in adults: diagnosis and management. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug 26. 86 p. (NICE guideline; no. 17).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2004 (updated 2015 Aug 26)

Guideline Developer(s)

National Clinical Guideline Centre - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Guideline Development Group (GDG)

Composition of Group That Authored the Guideline

Guideline Development Group Members: Stephanie Amiel (*Chair*), Professor of Diabetic Medicine King's College London; Augustin Brooks, Consultant Diabetologist, Bournemouth Hospital; Arthur Durrant, Patient member; Michael Flynn, Consultant Physician, Kent and Canterbury Hospital; Roger Gadsby, Visiting Professor, Institute for Diabetes in Older People, University of Bedfordshire, GP and Principal Teaching Fellow, University of Warwick; Peter Hammond, Consultant Physician, Harrogate District Hospital; Michael Kendall, Patient member; Vibhuti Mistry, Lead Diabetes and Obesity Dietitian, Homerton University Hospital NHS Foundation Trust; Henrietta Mulnier, Lecturer in Diabetes Nursing, King's College London; Victoria Ruszala, Specialist Pharmacist, Diabetes and Endocrinology, North Bristol NHS Trust; Stuart Smellie, Consultant in Chemical Pathology, Durham and Darlington NHS Foundation Trust; Perdy van den Berg, Clinical Lead, Oxfordshire Community Diabetes Service

Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Development Group (GDG) members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared arising conflicts of interest. Members were either required to withdraw completely or for part of the discussion if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Section 4.4, Declaration of Interests, in the original guideline

document and in Appendix B in the full guideline appendices (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: National Collaborating Centre for Chronic Conditions. Type 1 diabetes in adults. National clinical guideline for diagnosis and management in primary and secondary care. London (UK): Royal College of Physicians; 2004. 171 p. [382 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available in ePub or eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Type 1 diabetes in adults: diagnosis and management. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. 605 p. (NICE guideline; no. 17). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Type 1 diabetes in adults: diagnosis and management. Appendices A-F. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. 147 p. (NICE guideline; no. 17). Available from the NICE Web site .
- Type 1 diabetes in adults: diagnosis and management. Appendix G. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. 685 p. (NICE guideline; no. 17). Available from the NICE Web site.
- Type 1 diabetes in adults: diagnosis and management. Appendices H-U. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Dec. 642 p. (NICE guideline; no. 17). Available from the NICE Web site .
- Type 1 diabetes in adults: diagnosis and management. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. (NICE guideline; no. 17). Available from the NICE Web site .
- Type 1 diabetes in adults: diagnosis and management. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. 12 p. (NICE guideline; no. 17). Available from the NICE Web site .
- Type 1 diabetes in adults: diagnosis and management. Costing template. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. (NICE guideline; no. 17). Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .

Patient Resources

The following is available:

- Type 1 diabetes in adults: diagnosis and management. Information for the public. London (UK): National Institute for Care Excellence (NICE); 2015 Aug. (NICE guideline; no. 17). Available from the National Institute for Health and Care Excellence (NICE) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original

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NGC Status

This NGC summary was completed by ECRI on March 4, 2005. The information was verified by the guideline developer on September 29, 2006. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on January 10, 2008, following the U.S. Food and Drug Administration advisory on Carbamazepine. This summary was updated by ECRI Institute on April 1, 2009 following the FDA advisory on Reglan (metoclopramide). This summary was updated by ECRI Institute on May 1, 2009 following the U.S. Food and Drug Administration advisory on antiepileptic drugs. This summary was updated by ECRI Institute on November 13, 2015. This summary was updated by ECRI Institute on April 15, 2016 following the U.S. Food and Drug Administration advisory on Metformin-containing Drugs. This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on Opioid pain medicines.

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